

Type	L #	Hits	Search Text	DBs	Time Stamp	Com men ts	Error	Defin ition	Er rors
1	BRS	L1	25152 peptide same amphipathic same cationic sam alpha-helix	USPAT; US - PGPUB; EPO; JPO; DERWENT	2002/03/29 12:56				0
2	BRS	L2	95003 antimicrobial or antifungal or antiviral or parasite	USPAT; US - PGPUB; EPO; JPO; DERWENT	2002/03/29 12:57				0
3	BRS	L3	58 (peptide same amphipathic same cationic sam alpha-helix) same (antimicrobial or antifungal or antiviral or parasite)	USPAT; US - PGPUB; EPO; JPO; DERWENT	2002/03/29 12:57				0
4	BRS	L4	11 ((peptide same amphipathic same cationic sam alpha-helix) same (antimicrobial or antifungal or antiviral or parasite) same antibiotic	USPAT; US - PGPUB; EPO; JPO; DERWENT	2002/03/29 12:57				0
5	BRS	L5	0 ((peptide same amphipathic same cationic sam alpha-helix) same (bacterium or fungus or virus or parasite) same (multiple adj drug adj resistance)	USPAT; US - PGPUB; EPO; JPO; DERWENT	2002/03/29 12:58				0

Type	L #	Hits	Search Text	DBS	Time Stamp	Comments	Error	Definition	Errors
6	BRS L6	2	(( peptide same amphipathic same cationic sam alpha-helix ) same (bacterium or fungus or virus or parasite) ) same (gram adj positive adj bacterium)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/2 9 12:58		0		
7	BRS L7	5	(( peptide same amphipathic same cationic sam alpha-helix ) same (bacterium or fungus or virus or parasite) ) same (gram adj negative adj bacterium)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/2 9 12:58		0		
8	BRS L8	13	(( peptide same amphipathic same cationic sam alpha-helix ) same (antimicrobial or antifungal or antiviral or (parasite adj infection) ) ) or (( peptide same amphipathic same cationic sam alpha-helix ) same (bacterium or fungus 	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/2 9 12:59		0		

Type	L #	Hits	Search Text	DBs	Time Stamp	Com men ts	Error	Defin ition	Er rors
9	BRS	L9	penicillin, or cephalosporin or beta-lactam or amino glycoside or quinolone or tetracycline or macrolide or glycopeptide or lipopeptide or ( ribosome adj inhibitor)	USPAT; US - PGPUB; EPO; JPO; DERWENT	2002/03/2 9 13:00	0			
9		49832 5	(( peptide same amphiphatic same cationic sam alpha-helix ) same (antimicrobial or antifungal or antiviral or (parasite adj infection) ) or ( (peptide same amphiphatic same cationic sam alpha-helix ) same (bacterium or fungus or virus or parasite) ) same (penicillin, or cephalosporin or beta-lactam or amino glycoside or quinolone or tetracycline or macrolide or glycopeptide or lipopeptide or ( ribosome adj inhibitor))	USPAT; US - PGPUB; EPO; JPO; DERWENT	2002/03/2 9 13:00	0			
10	EBS	L10	70						

Type	L #	Hits	Search Text	DBs	Time Stamp	Com men ts	Error Defin itions	Error ro
11	BRS	L11	(peptide same amphipathic same cationic sam alpha-helix ) same parasite same malaria or trypanosomiosis	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/2 9 13:01		0	

(FILE 'HOME' ENTERED AT 13:04:41 ON 29 MAR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'  
ENTERED AT

13:05:06 ON 29 MAR 2002

L2 79 S PEPTIDE (P) AMPHIPATHIC (P) CATIONIC (P) ALPHA-HELIX

L3 465738 S ANTIMICROBIAL OR ANTIFUNGAL OR ANTIVIRAL OR  
PARASITE

L4 51 S L2 (P) L3

L5 18 DUPLICATE REMOVE L4 (33 DUPLICATES REMOVED)

L6 723744 S ANTIBIOTIC

L7 7 S L5 AND L6

L8 4036 S MULTIPLE DRUG RESISTANCE

L9 0 S L5 AND L8

=> log y

FILE 'HOME' ENTERED AT 13:04:41 ON 29 MAR 2002

=> file medline caplus biosis embase scisearch agricola  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 13:05:06 ON 29 MAR 2002

FILE 'CAPLUS' ENTERED AT 13:05:06 ON 29 MAR 2002  
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FILE 'AGRICOLA' ENTERED AT 13:05:06 ON 29 MAR 2002

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=> s peptide (p) amphipathic (p) cathionic (p) alpha-helix  
L1          0 PEPTIDE (P) AMPHIPATHIC (P) CATHIONIC (P) ALPHA-HELIX
```

=> s peptide (p) amphipathic (p) cationic (p) alpha-helix  
L2 79 PEPTIDE (P) AMPHIPATHIC (P) CATIONIC (P) ALPHA-HELIX  
  
=> s antimicrobial or antifungal orantiviral or parasite  
L3 465738 ANTIMICROBIAL OR ANTI FUNGAL OR ANTIVIRAL OR PARASITE

=> s 12 (p) 13  
L4 51 T2 (P) T3

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=> duplicate remove 14
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L4
L5          18 DUPLICATE REMOVE L4 (33 DUPLICATES REMOVED)
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==> d 15 1-18 ihib abs

L5 ANSWER 1 OF 18 MEDLINE DUPLICATE 1  
ACCESSION NUMBER: 2002127554 IN-PROCESS  
DOCUMENT NUMBER: 21839116 PubMed ID: 11751887  
TITLE: Trialysin, a novel pore-forming protein from saliva of hematophagous insects activated by limited proteolysis.  
AUTHOR: Amino Rogerio; Martins Rafael Miyazawa; Procopio Joaquim; Hirata Izaura Yoshico; Juliano Maria Aparecida; Schenkman Sergio  
CORPORATE SOURCE: Departamento de Microbiologia, Imunologia, e Parasitologia, Escola Paulista de Medicina, UNIFESP, Sao Paulo, S.P. 04023-062, Brazil.  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Feb 22) 277 (8) 6207-13.  
PUB. COUNTRY: Journal code: 2985121R. ISSN: 0021-9258.  
United States  
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)  
English  
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals  
OTHER SOURCE: GENBANK-AF427486; GENBANK-AF427487  
ENTRY DATE: Entered STN: 20020227  
Last Updated on STN: 20020227  
AB We have characterized a pore-forming lytic protein from the saliva of the hematophagous insect *Triatoma infestans*, a vector of Chagas disease. This protein, named trialysin, has 22 kDa and is present in the saliva at about

200 microg/ml. Purified trialysin forms voltage-dependent channels in planar lipid bilayers with conductance of 880 +/- 40 pS. It lyse protozoan \*\*\*parasites\*\*\* and bacteria indicating that it has a role in the control of microorganism growth in the salivary glands. At higher concentrations, but below those found in saliva, trialysin can also permeabilize and lyse mammalian cells, suggesting that it might also facilitate insect blood feeding by interfering with the cell response of the host. The translated cDNA sequence of trialysin shows a basic, lysine-rich protein in which the N-terminal region is predicted to form an \*\*\*amphipathic\*\*\* alpha-helical structure with positive charges on one side and hydrophobic amino acids on the opposite side. A synthetic \*\*\*peptide\*\*\* corresponding to this \*\*\*cationic\*\*\* \*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* induces protozoan lysis and mammalian cell permeabilization, showing that this region is involved in lytic activity. However, the lytic \*\*\*peptide\*\*\* G6V32 is 10-fold less efficient than trialysin in lysing \*\*\*parasites\*\*\* and 100-fold less efficient in permeabilizing mammalian cells. Trialysin activity is about 10-fold reduced in salivary gland homogenates prepared in the presence of an irreversible serine-protease inhibitor. Since trialysin precursor contains an anionic pro-sequence of 33 amino acids contiguous to the \*\*\*cationic\*\*\* \*\*\*amphipathic\*\*\* putative \*\*\*alpha\*\*\* - \*\*\*helix\*\*\*, we propose that removal of the acidic pro-sequence by limited proteolysis activates trialysin by exposing this lytic basic \*\*\*amphipathic\*\*\* motif.

L5 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:661637 CAPLUS

DOCUMENT NUMBER: 135:222359

TITLE: Expression of an antimicrobial peptide via the plastid genome to control phytopathogenic bacteria

INVENTOR(S): Daniell, Henry

PATENT ASSIGNEE(S): Auburn University, USA; University of Central Florida

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064927	A1	20010907	WO 2001-US6287	20010228
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-185662P P 20000229

AB This invention provides a novel method to confer disease resistance to plants. Plant plastids are transformed using a plastid vector which contains heterologous DNA sequences coding for a cytotoxic antimicrobial peptide. Transgenic plants are capable of fighting off phytopathogenic bacterial infection.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:617759 CAPLUS

DOCUMENT NUMBER: 135:185470

TITLE: Cationic, amphipathic .beta.-sheet peptides for antimicrobial use

INVENTOR(S): Blazyk, John F.

PATENT ASSIGNEE(S): Ohio University, USA

SOURCE: PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060162	A2	20010823	WO 2001-US4822	20010215
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				

PRIORITY APPLN. INFO.: US 2000-182495P P 20000215

AB This invention relates to an antimicrobial compd. which is (a) a peptide having a length of 8-50 amino acids, a net charge of at least four, a hydrophobic moment as a beta sheet which is at least 0.2 higher than its hydrophobic moment as an alpha helix, and having detectable membrane-disrupting activity against at least one microbial pathogen, and substantially no membrane disrupting activity against mammalian cells, or (b) a peptoid, peptidomimetic or nonpeptidic analog of a peptide according to (a) above. The antimicrobial use thereof is disclosed.

L5 ANSWER 4 OF 18 MEDLINE DUPLICATE 2  
 ACCESSION NUMBER: 2001436531 MEDLINE  
 DOCUMENT NUMBER: 21359369 PubMed ID: 11352918  
 TITLE: A novel linear amphipathic beta-sheet cationic antimicrobial peptide with enhanced selectivity for bacterial lipids.  
 AUTHOR: Blazyk J; Wiegand R; Klein J; Hammer J; Epand R M; Epand R F; Maloy W L; Kari U P  
 CORPORATE SOURCE: Department of Biomedical Sciences, College of Osteopathic Medicine, Ohio University, Athens, Ohio 45701, USA.. blazyk@ohio.edu  
 CONTRACT NUMBER: AI47165 (NIAID)  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Jul 27) 276 (30) 27899-906.  
 PUB. COUNTRY: United States  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200108  
 ENTRY DATE: Entered STN: 20010827  
 Last Updated on STN: 20010827  
 Entered Medline: 20010823

AB All known naturally occurring linear \*\*\*cationic\*\*\* \*\*\*peptides\*\*\* adopt an \*\*\*amphipathic\*\*\* alpha-helical conformation upon binding to lipids as an initial step in the induction of cell leakage. We designed an 18-residue \*\*\*peptide\*\*\*, (KIGAKI)3-NH<sub>2</sub>, that has no \*\*\*amphipathic\*\*\* character as an \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* but can form a highly \*\*\*amphipathic\*\*\* beta-sheet. When bound to lipids, (KIGAKI)3-NH<sub>2</sub> did indeed form a beta-sheet structure as evidenced by Fourier transform infrared and circular dichroism spectroscopy. The \*\*\*antimicrobial\*\*\* activity of this \*\*\*peptide\*\*\* was compared with that of (KIAGKIA)3-NH<sub>2</sub>, and it was better than that of GMASKAGAIAGKIAKVALKAL-NH<sub>2</sub> (PGLa) and (KLAGLAK)3-NH<sub>2</sub>, all of which form \*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* - \*\*\*helices\*\*\* when bound to membranes. (KIGAKI)3-NH<sub>2</sub> was much less effective at inducing leakage in lipid vesicles composed of mixtures of the acidic lipid, phosphatidylglycerol, and the neutral lipid, phosphatidylcholine, as compared with the other \*\*\*peptides\*\*\*. However, when phosphatidylethanolamine replaced phosphatidylcholine, the lytic potency of PGLa and the alpha-helical model \*\*\*peptides\*\*\* was reduced, whereas that of (KIGAKI)3-NH<sub>2</sub> was improved. Fluorescence experiments using analogs containing a single tryptophan residue showed significant differences between (KIGAKI)3-NH<sub>2</sub> and the alpha-helical \*\*\*peptides\*\*\* in their interactions with lipid vesicles. Because the data suggest enhanced selectivity between bacterial and mammalian lipids, linear \*\*\*amphipathic\*\*\* beta-sheet \*\*\*peptides\*\*\* such as (KIGAKI)3-NH<sub>2</sub> warrant further investigation as potential \*\*\*antimicrobial\*\*\* agents.

L5 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
 3

ACCESSION NUMBER: 2001:215682 BIOSIS  
 DOCUMENT NUMBER: PREV200100215682  
 TITLE: Linear \*\*\*cationic\*\*\* \*\*\*antimicrobial\*\*\* model

\*\*\*peptides\*\*\* with varying \*\*\*amphipathic\*\*\*  
\*\*\*alpha\*\*\* \*\*\*helix\*\*\* and beta-sheet potential.  
AUTHOR(S) : Blazyk, Jack (1); Hammer, Janet (1); Jin, Yi (1); Zhang, Yu  
(1); Zhu, Fang (1)  
CORPORATE SOURCE: (1) Ohio University, 234 Grosvenor, Athens, OH, 45701 USA  
SOURCE: Biophysical Journal, (January, 2001) Vol. 80, No. 1 Part 2,  
pp. 538a-539a. print.  
Meeting Info.: 45th Annual Meeting of the Biophysical  
Society Boston, Massachusetts, USA February 17-21, 2001  
Biophysical Society  
. ISSN: 0006-3495.

DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L5 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:519479 CAPLUS  
DOCUMENT NUMBER: 136:165482  
TITLE: Antimicrobial peptides - structure and function  
AUTHOR(S) : Mickowska, Barbara  
CORPORATE SOURCE: Zakl. Biochem. Anal., Inst. Biol. Molekularnej im.  
Jana Zurzyckiego, Uniw. Jagiellonski, Krakow, 31-120,  
Pol.  
SOURCE: Postepy Biologii Komorki (2001), 28(Supl. 16), 245-259  
CODEN: PBKODV; ISSN: 0324-833X  
PUBLISHER: Fundacja Biologii Komorki i Biologii Molekularnej  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Polish

AB A review. \*\*\*Antimicrobial\*\*\* \*\*\*peptides\*\*\* are part of the defense system mainly in plants and animals. In spite of great diversity of origin and amino acid compn., almost all of them are \*\*\*cationic\*\*\* (due to presence excess Arg and Lys residues) and the mols. form \*\*\*amphipathic\*\*\* structures. \*\*\*Antimicrobial\*\*\* \*\*\*peptides\*\*\* can be divided into several main groups based on their 3-dimensional structure: 1. Linear, forming . \*\*\*alpha\*\*\* . - \*\*\*helices\*\*\* ; 2. Antiparallel .beta.-sheets stabilized by intramol. disulfide bonds; 3. .alpha.-Helical and .beta.-sheet mixed structure with disulfide bonds; 4. Cyclic structures; and 5. Linear, with unusually high content of certain amino acid, often forming extended helices. \*\*\*Antimicrobial\*\*\* activity of these \*\*\*peptides\*\*\* is very broad, including bacteria, fungi, some protozoa, and even cancer cells. They are selectively toxic to microorganisms. Owing to the increasing resistance of bacteria to conventional antibiotics, \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* seem to be a promising source of antibiotics in future.

L5 ANSWER 7 OF 18 MEDLINE DUPLICATE 4  
ACCESSION NUMBER: 2001574646 MEDLINE  
DOCUMENT NUMBER: 21538640 PubMed ID: 11682065  
TITLE: Structural study of novel antimicrobial peptides, nigrocins, isolated from Rana nigromaculata.  
AUTHOR: Park S; Park S H; Ahn H C; Kim S; Kim S S; Lee B J; Lee B J  
CORPORATE SOURCE: Research Institute of Pharmaceutical Science, College of Pharmacy, Seoul National University, Seoul, South Korea.  
SOURCE: FEBS LETTERS, (2001 Oct 19) 507 (1) 95-100.  
Journal code: 0155157. ISSN: 0014-5793.

PUB. COUNTRY: Netherlands  
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: English  
ENTRY MONTH: Priority Journals  
200112

ENTRY DATE: Entered STN: 20011030  
Last Updated on STN: 20020123  
Entered Medline: 20011207

AB Novel \*\*\*cationic\*\*\* \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* , named nigrocin 1 and 2, were isolated from the skin of Rana nigromaculata and their amino acid sequences were determined. These \*\*\*peptides\*\*\* manifested a broad spectrum of \*\*\*antimicrobial\*\*\* activity against various microorganisms with different specificity. By primary structural analysis, it was revealed that nigrocin 1 has high sequence homology with brevinin 2 but nigrocin 2 has low sequence homology with any other known \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* . To investigate the structure-activity relationship of nigrocin 2, which has a unique primary

structure, circular dichroism (CD) and homonuclear nuclear magnetic resonance spectroscopy (NMR) studies were performed. CD investigation revealed that nigrocin 2 adopts mainly an alpha-helical structure in trifluoroethanol (TFE)/H<sub>2</sub>O solution, sodium dodecyl sulfate (SDS) micelles, and dodecylphosphocholine micelles. The solution structures of nigrocin 2 in TFE/H<sub>2</sub>O (1:1, v/v) solution and in SDS micelles were determined by homonuclear NMR. Nigrocin 2 consists of a typical

\*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* spanning residues 3-18 in both 50% TFE solution and SDS micelles. From the structural comparison of nigrocin 2 with other known \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\*, nigrocin 2 could be classified into the family of \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* containing a single linear \*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* that potentially disrupts membrane integrity, which would result in cell death.

L5 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:101949 CAPLUS

DOCUMENT NUMBER: 134:277651

TITLE: Antimicrobial host defense peptides: Action mechanisms and application

AUTHOR(S): Matsuzaki, Katsumi

CORPORATE SOURCE: Graduate School of Biostudies, Kyoto University, Yoshida-Shimoadachi-cho, Sakyo-ku, Kyoto, 606-8501, Japan

SOURCE: Foods & Food Ingredients Journal of Japan (2001), 190, 23-27

CODEN: FFIJER; ISSN: 0919-9772

PUBLISHER: FFI Janaru

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 22 refs. Animals defend themselves against invading pathogenic microorganisms, utilizing \*\*\*cationic\*\*\* \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\*, which rapidly kill various microbes without exerting toxicity against the host. Physicochem. \*\*\*peptide\*\*\* -lipid interactions provide attractive mechanisms for innate immunity. Many of these \*\*\*peptides\*\*\* form \*\*\*cationic\*\*\* \*\*\*amphipathic\*\*\* secondary structures, typically. \*\*\*alpha\*\*\* - \*\*\*helices\*\*\* and .beta.-sheets, which can selectively interact with anionic bacterial membranes by electrostatic means. This review summarizes various mechanisms of action for bacterial killing. Some \*\*\*peptides\*\*\* induce rapid permeabilization of cell membranes whereas others target intracellular nucleic acids. Several \*\*\*peptides\*\*\* are known to work synergistically. Finally, applications of these \*\*\*peptides\*\*\* are also discussed.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:113715 CAPLUS

DOCUMENT NUMBER: 130:163167

TITLE: Novel synthetic peptides with antimicrobial and endotoxin neutralizing properties for management of the sepsis syndrome

INVENTOR(S): Appelmelk, Bernard Jan; Abraham, Philip Richard; Van Deventer, Sander Jan Hendrik

PATENT ASSIGNEE(S): Academisch Ziekenhuis Bij de Universiteit van Amsterdam, Neth.

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906440	A1	19990211	WO 1997-NL449	19970731
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

RW: GH, KE, LS, MW, SD, SZ UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
GB, GR, IE, IT, LU, NL, PT, SE, BF, BJ, CF, CG, CI CM, GA,  
GN, ML, MR, NE, SN, TD, TG

AU 9737870 A1 19990222 AU 1997-37870 19970731

EP 988314 A1 20000329 EP 1997-934788 19970731

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

JP 2001512140 T2 20010821 JP 2000-505195 19970731

WO 1997-NL449 A 19970731

PRIORITY APPLN. INFO.:

MARPAT 130:163167

OTHER SOURCE(S):

AB A \*\*\*peptide\*\*\* with an amino acid compn. such that the \*\*\*peptide\*\*\* is \*\*\*amphipathic\*\*\*, \*\*\*cationic\*\*\* and forms a stable. \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* and has the following structure comprising .gtoreq.12 amino acids: R1-R2-A1-B1-(A2-B2-C1-A3)m-(C2)n-R3, wherein A = an amino acid selected from the basic amino acids Lys, Arg or His; B = an amino acid selected from the arom. amino acids Phe, Trp or Tyr; C = an amino acid selected from the group comprising the hydrophobic amino acids Leu, Ile, Val or Ala; and said \*\*\*peptide\*\*\* has either the orientation according to the formula or the retro orientation thereof, wherein at least 0-n of the repetitive sequence motifs (A2-B2-C1-A3) have the retro orientation and the remaining repetitive motifs (A2-B2-C1-A3) have the orientation as presented in the formula and wherein, R1, R2, and R3 are a no. of amino acids, said no. ranging 0-15 for each of the combination of R1 and R2 and for R3 and wherein m = 1-10, preferably 2-8, more preferably 2-5 and n = 1-3, a pharmaceutical compn. comprising such a \*\*\*peptide\*\*\* application thereof in treatment or diagnosis related to i.a. \*\*\*parasite\*\*\* infection topical and systemic tumors and septic shock.

REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 18 MEDLINE

DUPLICATE 5

ACCESSION NUMBER: 2000059353 MEDLINE

DOCUMENT NUMBER: 20059353 PubMed ID: 10590299

TITLE: Why and how are peptide-lipid interactions utilized for self-defense? Magainins and tachyplesins as archetypes.

AUTHOR: Matsuzaki K

CORPORATE SOURCE: Graduate School of Biostudies, Kyoto University,  
Yoshida-Shimoadachi-Cho 46-29, Sakyo-ku, Kyoto, Japan..  
katsumim@pharm.kyoto-u.ac.jp

SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Dec 15) 1462 (1-2)  
1-10. Ref: 78

Journal code: AOW; 0217513. ISSN: 0006-3002.

PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200002

ENTRY DATE: Entered STN: 20000218

Last Updated on STN: 20000218

Entered Medline: 20000208

AB Animals as well as plants defend themselves against invading pathogenic microorganisms utilizing \*\*\*cationic\*\*\* \*\*\*antimicrobial\*\*\*

\*\*\*peptides\*\*\*, which rapidly kill various microbes without exerting toxicity against the host. Physicochemical \*\*\*peptide\*\*\* -lipid interactions provide attractive mechanisms for innate immunity. Many of these \*\*\*peptides\*\*\* form \*\*\*cationic\*\*\* \*\*\*amphipathic\*\*\* secondary structures, typically \*\*\*alpha\*\*\* - \*\*\*helices\*\*\* and beta-sheets, which can selectively interact with anionic bacterial membranes by the aid of electrostatic interactions. Rapid, \*\*\*peptide\*\*\* -induced membrane permeabilization is an effective mechanism of

\*\*\*antimicrobial\*\*\* action. This review article summarizes interactions with lipid bilayers of magainins ( \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* ) and tachyplesins (beta-sheet) discovered in frog skin and horseshoe crab hemolymph, respectively, as archetypes, emphasizing that the mode of interaction is strongly dependent on the physicochemical properties not only of the \*\*\*peptide\*\*\*, but also of the target membrane.

L5 ANSWER 11 OF 18 MEDLINE

DUPLICATE 6

ACCESSION NUMBER: 1998190007 MEDLINE

DOCUMENT NUMBER: 98190007 PubMed ID: 9521752  
TITLE: Three-dimensional solution structure of lactoferricin B, an antimicrobial peptide derived from bovine lactoferrin.  
AUTHOR: Hwang P M; Zhou N; Shan X; Arrowsmith C H; Vogel H J  
CORPORATE SOURCE: Department of Biological Sciences, University of Calgary, Alberta, Canada.  
SOURCE: BIOCHEMISTRY, (1998 Mar 24) 37 (12) 4288-98.  
PUB. COUNTRY: United States  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199804  
ENTRY DATE: Entered STN: 19980507  
Last Updated on STN: 19980507  
Entered Medline: 19980430

AB The solution structure of bovine lactoferricin (LfcinB) has been determined using 2D 1H NMR spectroscopy. LfcinB is a 25-residue \*\*\*antimicrobial\*\*\* \*\*\*peptide\*\*\* released by pepsin cleavage of lactoferrin, an 80 kDa iron-binding glycoprotein with many immunologically important functions. The NMR structure of LfcinB reveals a somewhat distorted antiparallel beta-sheet. This contrasts with the X-ray structure of bovine lactoferrin, in which residues 1-13 (of LfcinB) form an \*\*\*alpha\*\*\* - \*\*\*helix\*\*\*. Hence, this region of lactoferricin B appears able to adopt a helical or sheetlike conformation, similar to what has been proposed for the amyloidogenic prion proteins and Alzheimer's beta- \*\*\*peptides\*\*\*. LfcinB has an extended hydrophobic surface comprised of residues Phe1, Cys3, Trp6, Trp8, Pro16, Ile18, and Cys20. The side chains of these residues are well-defined in the NMR structure. Many hydrophilic and positively charged residues surround the hydrophobic surface, giving LfcinB an \*\*\*amphipathic\*\*\* character. LfcinB bears numerous similarities to a vast number of \*\*\*cationic\*\*\* \*\*\*peptides\*\*\* which exert their \*\*\*antimicrobial\*\*\* activities through membrane disruption. The structures of many of these \*\*\*peptides\*\*\* have been well characterized, and models of their membrane-permeabilizing mechanisms have been proposed. The NMR solution structure of LfcinB may be more relevant to membrane interaction than that suggested by the X-ray structure of intact lactoferrin. Based on the solution structure, it is now possible to propose potential mechanisms for the \*\*\*antimicrobial\*\*\* action of LfcinB.

L5 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1998:588582 CAPLUS  
DOCUMENT NUMBER: 129:299443  
TITLE: Peptide-bilayer interactions:- simulation studies  
AUTHOR(S): La Rocca, Paolo; Sansom, Mark S. P.  
CORPORATE SOURCE: Laboratory of Molecular Biophysics, University of Oxford, Oxford, OX1 3QU, UK  
SOURCE: Biochem. Soc. Trans. (1998), 26(3), S302  
CODEN: BCSTB5; ISSN: 0300-5127

PUBLISHER: Portland Press Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A no. of \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* are believed to exert their action by forming \*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* - \*\*\*helices\*\*\* which assoc. with the cell membrane of the target organism, leading to its permeabilization and disruption. In order to understand the interaction of these \*\*\*peptides\*\*\* with membranes, methodologies are being developed to simulate their interaction with lipid bilayers. Here, two different modeling approaches are applied to simulate the membrane interaction of the \*\*\*cationic\*\*\* \*\*\*antimicrobial\*\*\* \*\*\*peptide\*\*\*, dermaseptin B, isolated from frog skin.

L5 ANSWER 13 OF 18 MEDLINE DUPLICATE 7  
ACCESSION NUMBER: 1998394846 MEDLINE  
DOCUMENT NUMBER: 98394846 PubMed ID: 9727863  
TITLE: Influence of preformed alpha-helix and alpha-helix induction on the activity of cationic antimicrobial peptides.  
AUTHOR: Houston M E Jr; Kondejewski L H; Karunaratne D N; Gough M; Fidai S; Hodges R S; Hancock R E  
CORPORATE SOURCE: Protein Engineering Network of Centres of Excellence,

University of Alberta, Edmonton, Canada.

JOURNAL OF PEPTIDE RESEARCH, (1998 Aug) 52 (2) -8.

Journal code: CTZ; 9707067. ISSN: 1397-002X.

SOURCE:

Denmark

Journal; Article; (JOURNAL ARTICLE)

PUB. COUNTRY:

English

LANGUAGE:

Priority Journals

FILE SEGMENT:

199811

ENTRY MONTH:

Entered STN: 19990106

ENTRY DATE:

Last Updated on STN: 19990106

Entered Medline: 19981124

AB One prominent class of \*\*\*cationic\*\*\* antibacterial \*\*\*peptides\*\*\* comprises the alpha-helical class, which is unstructured in free solution but folds into an \*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* upon insertion into the membranes of target cells. To investigate the importance of alpha-helicity and its induction on interaction with membranes, a series of \*\*\*peptides\*\*\* was constructed based on a hybrid of moth cecropin (amino acids 1-8) and bee melittin (amino acids 1-18) \*\*\*peptides\*\*\*. The new \*\*\*peptides\*\*\* were predicted to have a high tendency to form \*\*\*alpha\*\*\* - \*\*\*helices\*\*\* or to have preformed \*\*\*alpha\*\*\* - \*\*\*helices\*\*\* by virtue of construction of a lactam bridge between glutamate and lysine side-chains at positions i and i + 4 at various locations along the primary sequence. In two examples where the use of lactam bridge constraints induced and stabilized alpha-helical structure in benign (aqueous buffer) and/or hydrophobic medium, there was a decrease in antibacterial activity relative to the linear counterparts. Thus the preformation of \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* in solution was not necessarily beneficial to \*\*\*antimicrobial\*\*\* activity. In the one case where the lactam bridge did result in increased antibacterial activity (lower minimal inhibitory concentration values) it did not increase alpha-helical content in benign or hydrophobic medium. Broadly speaking, good activity of the \*\*\*peptides\*\*\* against Pseudomonas aeruginosa correlated best ( $r^2 = 0.88$ ) with a helican parameter which was calculated as the induction of \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* in a membrane-mimicking environment divided by the \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* formation under benign conditions. Interestingly, the activity of the lactam bridge \*\*\*peptide\*\*\* constructs correlated in part with alterations in bacterial outer or cytoplasmic membrane permeability.

L5 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2002 ACS

DUPLICATE 8

ACCESSION NUMBER: 1997:112231 CAPLUS

DOCUMENT NUMBER: 126:221637

TITLE:

Conformation and biological activity of mastoparan B and its analogs I

AUTHOR(S):

Park, Nam Gyu; Seo, Jung-Kil; Ku, Hee-Jung; Lee, Sannamu; Sugihara, Gohsuke; Kim, Kwang-Ho; Park, Jang-Su; Kang, Shin-Won

CORPORATE SOURCE:

Dep. Biotechnology & Bioengineering, Coll. Fisheries Sci., Pukyong National Univ., Pusan, 608-737, S. Korea

SOURCE:

Bull. Korean Chem. Soc. (1997), 18(1), 50-56

CODEN: BKCSDE; ISSN: 0253-2964

PUBLISHER:

Korean Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The mode of action of mastoparan B, an \*\*\*antimicrobial\*\*\* \*\*\*cationic\*\*\* tetradecapeptide amide isolated from the hornet Vespa basalis, toward phospholipid bilayers was studied with synthetic mastoparan B and its analogs with individual Ala instead of hydrophobic amino acids (1-Ile, 3-Leu, 6-Leu, 7-Val, 9-Trp, 13-Val, 14-Leu) in mastoparan B. Mastoparan B and its analogs were synthesized by the solid-phase method. CD spectra showed that mastoparan B and its analogs adopted an unordered structure in buffer soln. In the presence of neutral and acidic liposomes, most of the \*\*\*peptides\*\*\* took an alpha-helical structure. The calcein leakage expt. indicated that mastoparan B interacted strongly with neutral and acidic lipid bilayers than its analogs. Mastoparan B also showed a more or less highly \*\*\*antimicrobial\*\*\* activity and hemolytic activity for human erythrocytes than its analogs. These results indicate that the hydrophobic face in the \*\*\*amphipathic\*\*\* . \*\*\*alpha\*\*\* . - \*\*\*helix\*\*\* of mastoparan B critically affect biol. activity and helical contents.

L5 ANSWER 15 OF 18 MEDLINE                          DUPLICATE

ACCESSION NUMBER: 97102718 MEDLINE  
DOCUMENT NUMBER: 97102718 PubMed ID: 8946958  
TITLE: Solution structure of an antimicrobial peptide buforin II.  
AUTHOR: Yi G S; Park C B; Kim S C; Cheong C  
CORPORATE SOURCE: Magnetic Resonance Group, Korea Basic Science Institute, Taejon, South Korea.  
SOURCE: FEBS LETTERS, (1996 Nov 25) 398 (1) 87-90.  
Journal code: EUH; 0155157. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199701  
ENTRY DATE: Entered STN: 19970219  
Last Updated on STN: 19970219  
Entered Medline: 19970122

AB The structure of 21-residue \*\*\*antimicrobial\*\*\* \*\*\*peptide\*\*\* buforin II has been determined by using NMR spectroscopy and restrained molecular dynamics. Buforin II adopts a flexible random structure in H<sub>2</sub>O. In trifluoroethanol (TFE)/H<sub>2</sub>O (1:1, v/v) mixture, however, buforin II assumes a regular \*\*\*alpha\*\*\* - \*\*\*helix\*\*\* between residues Val12 and Arg20 and a distorted helical structure between residues Gly7 and Pro11. The model structure obtained shows an \*\*\*amphipathic\*\*\* character in the region from Arg5 to the C-terminus, Lys21. Like other known \*\*\*cationic\*\*\* \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\*, the \*\*\*amphipathic\*\*\* structure might be the key factor for \*\*\*antimicrobial\*\*\* activity of buforin II.

L5 ANSWER 16 OF 18 MEDLINE                          DUPLICATE 10

ACCESSION NUMBER: 95255306 MEDLINE  
DOCUMENT NUMBER: 95255306 PubMed ID: 7737198  
TITLE: PMAP-37, a novel antibacterial peptide from pig myeloid cells. cDNA cloning, chemical synthesis and activity.  
AUTHOR: Tossi A; Scocchi M; Zanetti M; Storici P; Gennaro R  
CORPORATE SOURCE: Dipartimento di Biochimica, Biofisica e Chimica delle Macromolecole, Universita di Trieste, Italy.  
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1995 Mar 15) 228 (3) 941-6.  
Journal code: EMZ; 0107600. ISSN: 0014-2956.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-L39641  
ENTRY MONTH: 199506  
ENTRY DATE: Entered STN: 19950615  
Last Updated on STN: 19980206  
Entered Medline: 19950602

AB A molecular biological approach, based on preproregion homology in the precursors of several diverse antibacterial \*\*\*peptides\*\*\*, was used to clone a pig bone marrow cDNA encoding a novel 167-residue polypeptide. The preproregion of this polypeptide is highly similar to corresponding regions in congeners from pig, cattle and rabbit. It is followed by a unique, \*\*\*cationic\*\*\*, 37-residue sequence, which was predicted to have a high propensity for an alpha-helical conformation. A \*\*\*peptide\*\*\*, termed PMAP-37, corresponding to this sequence, was chemically synthesized and shown to undergo a transition from a random coil to an ordered, mainly helical, conformation on addition of trifluoroethanol. This behaviour is typical of an \*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* \*\*\*helix\*\*\*, a structure common to several membrane-active, \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\*. In vitro experiments showed that PMAP-37 strongly inhibits the growth of several strains of Gram-negative and Gram-positive bacteria, with minimal inhibitory concentrations ranging over 1-4 microM, and permeabilizes the inner membrane of Escherichia coli. Interestingly, the 15-32 stretch of PMAP-37 show a remarkable similarity to N-terminal stretches in cecropins B and A from Drosophila melanogaster and Cecropia hyalophora, respectively. This affords an uncommon example of sequence convergence.

L5 ANSWER 17 OF 18 MEDLINE                          DUPLICATE 11

ACCESSION NUMBER: 94139686 MEDLINE  
DOCUMENT NUMBER: 94139686 PubMed ID: 8306981  
TITLE: Isolation and structure of novel defensive peptides from frog skin.  
AUTHOR: Mor A; Nicolas P  
CORPORATE SOURCE: Laboratoire de Bioactivation des Peptides, Institut Jacques Monod, France.  
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1994 Jan 15) 219 (1-2)  
145-54.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-P80277; GENBANK-P80278; GENBANK-P80279;  
GENBANK-P80280; GENBANK-P80281; GENBANK-P80282;  
GENBANK-P80283  
ENTRY MONTH: 199403  
ENTRY DATE: Entered STN: 19940330  
Last Updated on STN: 19980206  
Entered Medline: 19940317

AB In addition to the highly specific cell-mediated immune system, vertebrates possess an efficient host-defense mechanism against invading microorganisms which involves the synthesis of highly potent \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* with a large spectrum of activity. A 34-residue \*\*\*cationic\*\*\* and amphipathic \*\*\*peptide\*\*\*, designated dermaseptin I, was recently isolated from the skin of the arboreal frog *Phyllomedusa sauvagii* and was shown to exhibit microbicidal activity against various pathogenic microorganisms including bacteria, yeast, protozoa and filamentous fungi. In this study, we report the isolation and characterization of four novel \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* from frog skin through the combined use of an anti-dermaseptin enzyme immunoassay and an antifungal bioassay. The 28-34-residue \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* are \*\*\*cationic\*\*\*, containing 3-5 lysine residues that punctuate an alternating hydrophobic and hydrophilic sequence. Based on their primary structure, all four \*\*\*peptides\*\*\* can be fitted to a class L \*\*\*amphipathic\*\*\* \*\*\*alpha\*\*\* \*\*\*helix\*\*\* which places all lysine residues on the polar side of the helix. The four \*\*\*antimicrobial\*\*\* \*\*\*peptides\*\*\* have high sequence similarity with dermaseptin I (53-94% similarity) suggesting that their respective genes are all members of the same family. In addition, pairwise sequence alignment of dermaseptin I and adenoregulin, a 33-residue \*\*\*cationic\*\*\* \*\*\*peptide\*\*\* recently isolated from frog skin and shown to enhance the binding of agonists to the A1 adenosine receptor, reveals 62% similarity (39% amino acid positional identity). Both \*\*\*peptides\*\*\* share a similar but non-identical spectrum of \*\*\*antimicrobial\*\*\* activity, being active against bacteria, yeast and filamentous molds. However, no significant hemolytic activity was found for these \*\*\*peptides\*\*\* which suggests a selectivity for prokaryotic cells. These findings indicate that adenoregulin should be included in the dermaseptin family of \*\*\*peptides\*\*\*. In addition, tryptic digestion of purified pro-dermaseptin I liberated a 15-amino-acid \*\*\*peptide\*\*\* identified as the authentic C-terminus of dermaseptin I. These results are in accordance with the predicted sequences of pro-dermaseptins obtained through molecular cloning, in which the dermaseptin progenitor sequences are located at the extreme C-terminus of the precursors.

L5 ANSWER 18 OF 18 MEDLINE DUPLICATE 12  
ACCESSION NUMBER: 92078177 MEDLINE  
DOCUMENT NUMBER: 92078177 PubMed ID: 1744108  
TITLE: Bombinin-like peptides with antimicrobial activity from skin secretions of the Asian toad, *Bombina orientalis*.  
AUTHOR: Gibson B W; Tang D Z; Mandrell R; Kelly M; Spindel E R  
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of California, San Francisco 94143-0446.  
CONTRACT NUMBER: CA39237 (NCI)  
RR01614 (NCRR)  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Dec 5) 266 (34)  
23103-11.  
PUB. COUNTRY: Journal code: HIV; 2985121R. ISSN: 0021-9258.  
United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

OTHER SOURCE:

GENBANK-M55199; GENBANK-M55200; GENBANK-M55201;

GENBANK-M76483; GENBANK-M76484; GENBANK-M96682;

GENBANK-S66610; GENBANK-S66768; GENBANK-S68993;

GENBANK-S70582

ENTRY MONTH:

199201

ENTRY DATE:

Entered STN: 19920202

Last Updated on STN: 19920202

Entered Medline: 19920113

AB The structures and hemolytic and bactericidal activities of three bombinin-like \*\*\*peptides\*\*\*, or BLP-1-3, from the skin of *Bombina orientalis* are described. The \*\*\*peptides\*\*\* were isolated from the skin of *B. orientalis* and sequenced by tandem mass spectrometry and are \*\*\*amphipathic\*\*\*, \*\*\*cationic\*\*\* \*\*\*peptides\*\*\* of 25-27 amino acids in length. The sequence of the most abundant member (BLP-1) is: Gly-Ile-Gly-Ala-Ser-Ile-Leu-Ser-Ala-Gly-Lys-Ser-Ala-Leu-Lys-Gly-Leu-Ala-Lys-Gly-Leu-Ala-Glu-His-Phe-Ala-Asn-NH<sub>2</sub>. All three \*\*\*peptides\*\*\* were found to share considerable, but not complete, homology with bombinin, an \*\*\*antimicrobial\*\*\*, hemolytic \*\*\*peptide\*\*\* first isolated by Michl and Csordas (Csordas, A., and Michl, A. (1970) Monatsh. Chem. 101, 182-189) from the skin of *Bombina variegata*. The BLPs have been assayed for antibiotic and hemolytic activity and found to be more potent than magainin 2 (a related \*\*\*antimicrobial\*\*\* \*\*\*peptide\*\*\* from *Xenopus laevis*) in their ability to kill bacteria. However, no significant hemolytic activity was found for these \*\*\*peptides\*\*\* which suggests a selectivity for prokaryotic over eukaryotic membranes. The molecular basis for antibacterial activity is presumed to be due to their predicted \*\*\*amphipathic\*\*\* alpha-helical structures which is supported by circular dichroism measurements that found significant helical content (63-69% \*\*\*alpha\*\*\* - \*\*\*helix\*\*\*) in 40% trifluoroethanol. Last, a cDNA library was constructed from the skin of *B. orientalis* and screened with an oligonucleotide probe complementary to the COOH terminus of BLP-1. Several clones were isolated and sequenced that encode BLP-1 and BLP-3, as well as an additional \*\*\*peptide\*\*\* (BLP-4) that differs by two amino acid substitutions from BLP-3.

=> s antibiotic

L6 723744 ANTIBIOTIC

=> d his

(FILE 'HOME' ENTERED AT 13:04:41 ON 29 MAR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
13:05:06 ON 29 MAR 2002

L1 0 S PEPTIDE (P) AMPHIPATHIC (P) CATHIONIC (P) ALPHA-HELIX

L2 79 S PEPTIDE (P) AMPHIPATHIC (P) CATIONIC (P) ALPHA-HELIX

L3 465738 S ANTIMICROBIAL OR ANTIFUNGAL ORANTIVIRAL OR PARASITE

L4 51 S L2 (P) L3

L5 18 DUPLICATE REMOVE L4 (33 DUPLICATES REMOVED)

L6 723744 S ANTIBIOTIC

=> s 15 and 16

L7 7 L5 AND L6

=> s multiple drug resistance

4 FILES SEARCHED...

L8 4036 MULTIPLE DRUG RESISTANCE

=> s 15 and 18

L9 0 L5 AND L8

=> d his

(FILE 'HOME' ENTERED AT 13:04:41 ON 29 MAR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
13:05:06 ON 29 MAR 2002

L1 0 S PEPTIDE (P) AMPHIPATHIC (P) CATHIONIC (P) ALPHA-HELIX

L2 79 S PEPTIDE (P) AMPHIPATHIC (P) CATIONIC (P) ALPHA-HELIX  
L3 465738 S ANTIMICROBIAL OR ANTIFUNGAL OR ANTIVIRAL OR PARASITIC  
L4 51 S L2 (P) L3  
L5 18 DUPLICATE REMOVE L4 (33 DUPLICATES REMOVED)  
L6 723744 S ANTIBIOTIC  
L7 7 S L5 AND L6  
L8 4036 S MULTIPLE DRUG RESISTANCE  
L9 0 S L5 AND L8

=> log y

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